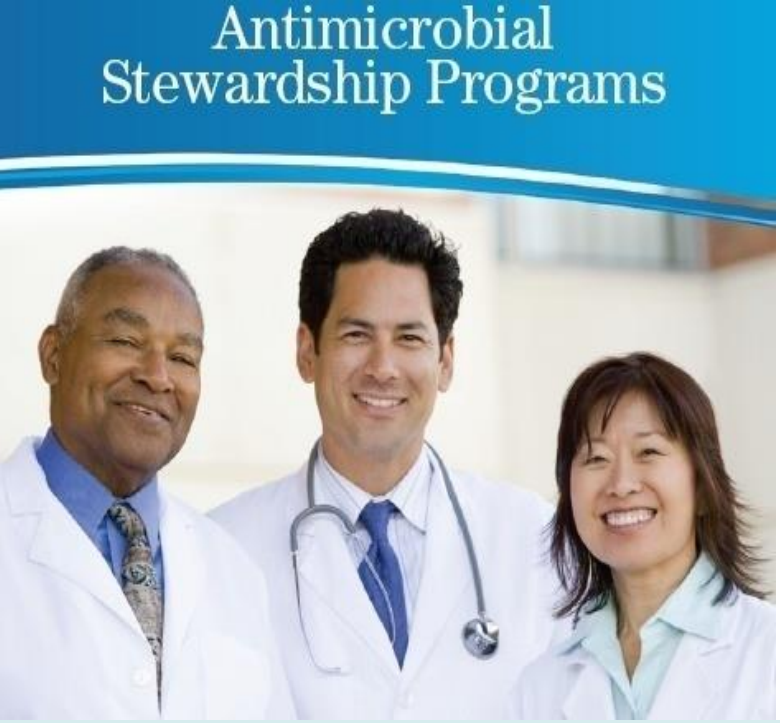


Antimicrobial Stewardship:

Arizona Partnerships Working to Improve the Use of Antimicrobials in the Hospital and Community

Part 5

"Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence."

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

"…we hold closely the principles that antibiotics are a gift to us from prior generations and that we have a moral obligation to ensure that this global treasure is available for our children and future generations."

- David Gilbert, et al (and the Infectious Diseases Society of America). Clin Infect Dis. 2010;51:754-5

A Note To Our Readers and Slide Presenters

The objectives of the Subcommittee on Antimicrobial Stewardship Programs are directed at education, presentation, and identification of resources for clinicians to create toolkits of strategies that will assist clinicians with understanding, implementing, measuring, and maintaining antimicrobial stewardship programs.

The slide compendium was developed by the Subcommittee on Antimicrobial Stewardship Programs (ASP) of the Arizona Healthcare-Associated Infection (HAI) Advisory Committee in 2012-2013.

ASP is a multidisciplinary committee representing various healthcare disciplines working to define and provide guidance for establishing and maintaining an antimicrobial stewardship programs within acute care and long-term care institutions and in the community.

Their work was guided by the best available evidence at the time although the subject matter encompassed thousands of references. Accordingly, the Subcommittee selectively used examples from the published literature to provide guidance and evidenced-based criteria regarding antimicrobial stewardship. The slide compendium reflects consensus on criteria which the HAI Advisory Committee deems to represent prudent practice.

Disclaimers

All scientific and technical material included in the slide compendium applied rigorous scientific standards and peer review by the Subcommittee on Antimicrobial Stewardship Programs to ensure the accuracy and reliability of the data. The Subcommittee reviewed hundreds of published studies for the purposes of defining antimicrobial stewardship for Arizonan clinicians. The Arizona Department of Health Services (ADHS) and members of its subcommittees assume no responsibility for the opinions and interpretations of the data from published studies selected for inclusion in the slide compendium.

ADHS routinely seeks the input of highly qualified peer reviewers on the propriety, accuracy, completeness, and quality (including objectivity, utility, and integrity) of its materials. Although the specific application of peer review throughout the scientific process may vary, the overall goal is to obtain an objective evaluation of scientific information from its fellow scientists, consultants, and Committees.

Please credit ADHS for development of its slides and other tools. Please provide a link to the ADHS website when these material are used.

Introduction to Slide Section

- **Preface:**

  Measuring antimicrobial use is essential in any ASP. However, even today, many technologies are not amenable to providing accurate data. Targeted antimicrobials as well as overall use should be considered for tracking utilization. Defined daily doses are frequently discussed but other measures of antimicrobial use are also useful. The measures used should reflect the program's goals but also should permit benchmarking. Appropriate adjustment for census and patient location are important. mandatory.

- **Content:**

  12 slides

- **Suggestions for Presentation:**

  This slide section may be used for education, self-study, or presentation to the stewardship committee and pharmacy director. The ASP should study each potential measure and decide how each plays a role in tracking usage while assessing the time and labor involved in collecting such data.

- **Comments:**

  Measures of antimicrobial use are frequently equated to bacterial resistance. However, proving biologic causality between use and resistance is elusive since institutional resistance, as revealed on antibiograms, is composed of several influences including antimicrobial use in the community and long-term care institutions.

ANTIMICROBIAL STEWARDSHIP: MEASURING ANTIBIOTIC UTILIZATION

Measuring Antimicrobial Use

- Surveillance of antimicrobial use allows targeting of areas with high or increased use of specific agents
  - Perform at least annually
  - Stratify by antibiotic agent
  - Create data for hospital units, medical service, or specific providers
- Normalize antibiotic use data (measure rate of use) to account for fluctuations in length of stay and patient census
  - Per 1,000 patient days
    - Normalizes antibiotic use for decreased length of stay and census
    - Avoids a “perceived decrease” in antibiotic use unless antibiotic use is adjusted by an appropriate denominator
  - Per admission or discharge
    - Affected by patients in observation status, which may not be regarded as admissions
- Assess changes in antibiotic use after interventions
  - Important to look at all classes of antibiotics – are providers just substituting one agent for another? (Example: ertapenem + tobramycin in place of meropenem for empiric coverage of *Pseudomonas* plus ESBLs when meropenem but not ertapenem is restricted)

Measuring Antibiotic Use: Data Sources

- Data measurement depends on purpose
  - Assessment of individual hospital costs and consumption
  - Comparison with similar institutions
  - Resistance to antimicrobial agents

Source	Advantage	Disadvantage
Cost-based methodologies, such as hospital purchase data	• Easy data to obtain • Grams purchased over time can be converted to other units of measure, e.g., DDDs	• Loses accuracy as price fluctuates, such as generic entries, price contracting • Stock may be sitting on shelf • Month-to-month stock turnover • Size of inventory
Pharmacy dispensing data	• Surrogate for what is actually administered	• Incorrect billing • Credit of returned doses
Antibiotic administration data	• Most accurate data • Bar coding at point of care is better than charting on MAR	• Most difficult to obtain

Basics of Antibiotic Use Metrics: DDD vs PDOT

- Defined daily dose (DDD)
  - The usual adult daily dose defined by the World Health organization (WHO)
  - Problems: does not consider renal dose adjustment; WHO has changed DDD for some drugs; does not consider number of patients exposed to drug
  - Adjusted for hospital census, i.e., per 1,000 patient days (pt-days)
  - Example:
    - Vancomycin, 1.0 DDD = 2 grams
    - A patient who receives 1 gm BID = 1.0 DDD; 5 days of treatment = 5.0 DDDs
- Patient days of therapy (PDOT)
  - 1.0 DOT is the administration of at least one dose of a single agent on a given day
  - Problems: it is unclear number of patients who receive the drug
  - Insensitive to renal function and dosage; simply one day of exposure
  - Can be adjusted for hospital census, i.e., per 1,000 patient days (pt-days)
  - Example:
    - One patient receives vancomycin 1 gram Q12H x 5 days = 5 PDOTs
    - Another patient receives vancomycin 1 gram Q24H x 5 days = 5 PDOTs

Basics of Antibiotic Use Metrics: DDD vs DOT

- Defined daily dose (DDD)
  - The usual adult daily dose defined by the World Health organization (WHO)
  - Example:
    - Vancomycin, 1.0 DDD = 2 grams (1 gm BID or 2 grams daily)
    - A patient who receives 1 gm BID x 5 days = 5.0 DDDs
    - A patient who receives 500 mg BID x 5 days = 1 gm x 5 days = 5 gms (divided by 2 gms usual adult daily dose) = 2.5 DDDs
    - A hospital "uses" 1,000 gm of vancomycin (e.g. purchases, dispenses, or administers) in the first quarter of the year for 4,500 patient days, then: (1000 gm/2 gm/4,500 patient days) x 1,000 = 111 DDD/1,000 patient days
- Days of therapy (DOT)
  - 1.0 DOT represents the administration of a single agent on a given day regardless of the number of doses administered or dosage strength; in essence, 1.0 DOT is the administration of at least one dose of a single agent on a given day
  - Example:
    - A patient receives vancomycin 1 gram Q12H x 5 days = 5 DOTs
    - Another patient receives vancomycin 1 gram Q24H x 5 days = 5 DOTs
    - One patient receives ceftriaxone 1 gm Q24H x 5 days and azithromycin 500 mg Q24H x 5 days = 10 DOTs (each drug is counted separately)

Polk R et al. Clin Infect Dis. 2007;44:664-70

Measuring Antibiotic Use: DDD versus DOT

Method	Advantages	Disadvantages
Defined daily dose (DDD)	• Standardized comparisons among hospitals or countries • Can be used where limited access to computerized pharmacy data exists (does not require order level data)	• DDD may not represent appropriate dose for the specific infection being treated • Poor estimate in pediatrics • Underestimates usage for drugs that are renally adjusted • Is not sensitive to drugs commonly used for surgical prophylaxis • Approved DDD may change as new dosages are approved
Days of therapy (DOT)	• Can be used in pediatrics • Not influenced by discrepancies of prescribed daily dose or assigned DDD • Not influenced by changes in the recommended DDD	• Overemphasizes appropriate multi-drug regimens • Does not resolve all renal dosing issues, e.g., vancomycin Q3 days in severe renal dysfunction (1 DOT every 3 days, what is duration of exposure?) • Difficult to measure, even with computerized pharmacy records • Time-consuming

A Potential Useful New Measure: Length of Therapy (LOT)

- Can be used to complement days of therapy (DOT)
- Hospitals that use more combination therapy will have higher DOTs than those that use monotherapy, but LOT should be the same
  - Ciprofloxacin + metronidazole x 5 days = 10 DOTs, 5 LOTs
  - Ertapenem x 5 days = 5 DOTs, 5 LOTs
- DOT ÷ LOT – measures the number of antimicrobial agents administered per patient per day
- Mean DOT or LOT per discharge or DOT or LOT per 1,000 patient-days provide a more complete picture of antimicrobial use when applied to different medical services within the hospital
- When the DOT or LOT values per 1,000 patient-days are risk-adjusted by case-mix index (CMI) inter-hospital comparisons can be made (cautiously)

Ibrahim O, Polk R. Expert Rev Anti Infect Therapy. 2012;10:445-7

Benchmarking Antimicrobial Use: Current Issues

- The most appropriate metric for measuring antibacterial drug use for benchmarking purposes remains a matter of considerable debate
- Benchmarking may identify outliers, both high and low, so that best practice strategies can be identified and implemented to improve patient care
  - Risk adjustment is used to control for interhospital differences in case mix that otherwise confound comparisons, such as case mix index (CMI), bed size, academic vs community hospital, and transplant services
  - Benchmarking can be done through reporting to the National Healthcare Safety Network – Antimicrobial Use and Resistance module (NHSN AUR module) or the University HealthSystem Consortium (UHC)

Polk R et al. Clin Infect Dis. 2011;53(11):1100-10.

Are There Antibiotic Use Metric Data Available For The USA?

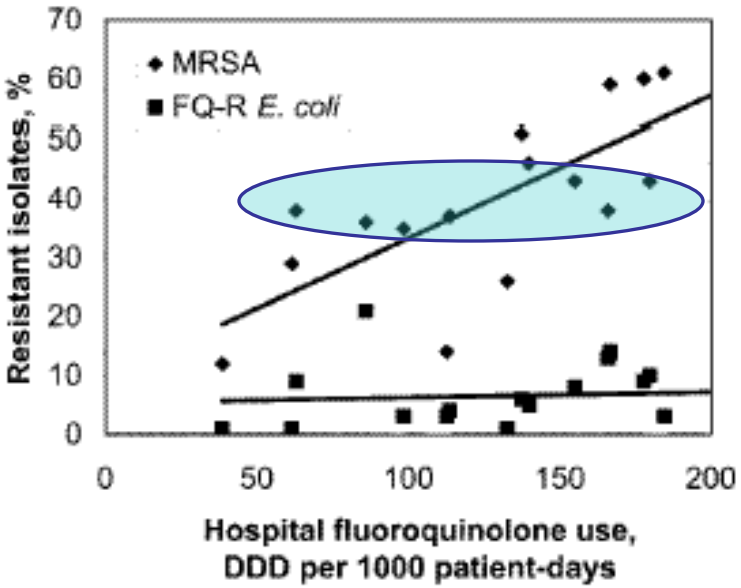
- Use of 50 antibacterial drugs administered to adults discharged from 130 US hospitals between August 1, 2002 and July 31, 2003
- Of 1,795,504 patients, 59.8% received at least 1 dose of an antibacterial drug
- The mean (± SD) of total antibacterial drug use measured by the number of DDDs per 1000 patient-days and the number of DOTs per 1000 patient-days were not significantly different, although the correlation was poor

Parenteral Agent	No. of hospitals	Mean DDDs/1,000 pt-days (± SD)	Mean DOTs/1,000 pt-days (± SD)	Mean administered daily dose, g/d
Cefazolin	130	80.3 ± 35.4	94.3 ± 27.7	2.46
Ciprofloxacin	123	18.0 ± 22.1	13.5 ± 16.3	0.72
Levofloxacin	123	75.6 ± 57.5	74.9 ± 55.8	0.51
Ceftriaxone	130	44.9 ± 28.2	62.9 ± 35.9	1.46
Vancomycin	130	46.1 ± 39.0	52.7 ± 26.6	1.63
Pip-tazobactam	127	30.3 ± 20.3	42.7 ± 28.5	10.1
Metronidazole	126	28.1 ± 14.3	32.8 ± 15.4	1.32
Azithromycin	130	20.8 ± 17.1	18.0 ± 14.8	0.55

Polk R et al. Clin Infect Dis 2007; 44:664-70.

Is Antimicrobial Use Data Correlated With Bacterial Resistance?

- Measurement of fluoroquinolone (FQ) use in 17 U.S. hospitals during 2000
- Fluoroquinolone use (DDD/1,000 pt-days) correlated with %MRSA, but not FQ-resistant *E. coli*
- Questions:
  - Why does a 4-fold difference in hospital FQ use density produce similar rates of MRSA within the range of 30% to 45% (blue oval)?
  - Why does hospital FQ use not translate into changes in resistance?
  - How do patient demographics relate to antibiotic resistance, beyond antibiotic exposure?
  - Is resistance being imported into the hospital?



Mathematical Correlations Between Antibiotic Use and Bacterial Resistance May Not Infer Biological Causality When Other Important Demographic Factors Are Not Considered

MacDougall C, et al. Clin Infect Dis. 2005;41:435-40

Measuring Antimicrobial Use: Summary and Considerations

- Measure something: DDD, DOT, LOT
- Normalize data to account for fluctuations in patient volume
- Trend data over time
- Trend specific agents
  - Usually for the whole institution but may be useful to trend by unit or service
- Antibiotic use per indication or per syndrome
- Review antimicrobial use at group or individual prescriber level
- Consider service-specific reports
  - Intensive care unit
  - Solid organ transplant
  - Bone marrow transplant
- Consider reporting antifungal and antiviral agents separately
- Consider reporting antimicrobial use for benchmarking (e.g. NHSN AUR)